I. AMENDMENT

Amendments to the Specification:

At page 2, please delete the paragraph spanning lines 2-5.

Listing of claims:

1.-29. (Cancelled)

30. (Currently amended) A recombinant adenovirus composition comprising between 5 x 10^{14} and 1 x 10^{18} viral particles, prepared by a process comprising ~~in accordance with claim 1.~~

(a) preparing a culture of producer cells in a selected media;

(b) infecting producer cells in the culture with recombinant adenovirus, wherein the producer cells are infected between mid-log phase of growth and stationary phase of growth; and

(c) harvesting recombinant adenovirus from the cell culture.

31. (Currently amended) ~~A~~ The purified recombinant adenovirus composition ~~comprising between 5 x 10^{14} and 1 x 10^{18} adenoviral particles~~ of claim 30 or 41, said composition having one or more of the following properties:

(a) a virus titer of between about 1 x 10^{9} and about 1 x 10^{13} pfu/ml;

(b) a virus particle concentration between about 1 x 10^{10} and about 2 x 10^{13} particles/ml;

(c) a particle:pfu ratio between about 10 and about 60;

(d) having less than 50 ng BSA per 1 x ~~10e12~~ 10^{12} viral particles;

(e) between about 50 pg and 1 ng of contaminating human DNA per 1 x 10^{12} viral particles,

(f) elutes essentially as a single elution peak upon HPLC.

32. (Currently amended) The composition of claim 30 or 41 ~~31~~, wherein the composition has a viral titer of between about 1×10^{11} and about 1×10^{13} pfu/ml.

33. (Original) The composition of claim 32, wherein the composition has a viral titer of between about 1×10^{12} and about 1×10^{13} pfu/ml.

34. (Currently amended) The composition of claim 30 or 41 ~~31~~, wherein the composition has a virus particle concentration between about 1×10^{11} and about 2×10^{13} particles/ml.

35. (Currently amended) The composition of claim 34, wherein the composition has a virus particle concentration between about 1×10^{12} and about 1×10^{13} particles/ml.

36. (Currently amended) The composition of claim 30 or 41 ~~31~~, wherein the composition has a particle:pfu ratio between about 10 and about 50.

37. (Original) The composition of claim 36, wherein the composition has a particle:pfu ratio between about 10 and about 40.

38. (Original) The composition of claim 37, wherein the composition has a particle:pfu ratio between about 20 and about 40.

39. (Currently amended) The composition of claim 30 or 41 ~~31~~, wherein the composition has between about 1 ng and 50 ng BSA per 1×10^{12} viral particles.

40. (Original) The composition of claim 39, wherein the composition has between about 5 ng and 40 ng BSA per 1×10^{12} viral particles.

41. (Currently amended) A purified recombinant adenovirus composition comprising between 5 x 10^{14} and 1 x 10^{18} adenoviral particles and ~~The composition of claim 31, wherein the composition has~~ between about 50 pg and 500 pg of contaminating human DNA per 1 x 10^{12} viral particles.

42. (Currently amended) The composition of claim 30 or 41, wherein the composition has between about 100 pg and 500 pg of contaminating human DNA per 1 x 10^{12} viral particles.

43. (Original) The composition of claim 30 or 41 ~~31~~, wherein the adenovirus of said composition elutes as essentially a single HPLC peak that comprises between 97 and 99% of the total area under the peak.

44. (New) The composition of claim 30 or 41, wherein the composition has between about 50 pg and about 7 ng of contaminating human DNA per 1 x 10^{12} viral particles.

45. (New) The composition of claim 44, wherein the composition has between about 50 pg and about 5 ng of contaminating human DNA per 1 x 10^{12} viral particles.

46. (New) The composition of claim 45, wherein the composition has between about 50 pg and about 3 ng of contaminating human DNA per 1 x 10^{12} viral particles.

47. (New) The composition of claim 46, wherein the composition has between about 50 pg and about 1 ng of contaminating human DNA per 1 x 10^{12} viral particles.

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 30-43 were pending prior to the Office Action dated October 3, 2003. Claim 30 has been amended into independent claim format so that it no longer depends from claim 1, which was previously cancelled. Claim 41 was also amended from dependent claim format into independent claim format, as this claim was found to be free of the prior art.[1] Claim 31 has been amended to depend from claim 41, and claims 44-47 have been added. The amended claims and the added claims should similarly be free of the prior art as they recite purity limitations that are consistent with claim 41. Support for the amendments and the added claims can be in the originally filed claims and throughout the specification, for example, at page 99, line 30 to page 100, line 8. No new matter has been added.

B. No Filing on March 28, 2003

On page 2 of the Action, an inquiry is made regarding an entry on the list of file contents regarding "Pet. 1.53" on March 28, 2003. Applicants' representative is unaware of any such paper or any filing on or near March 28, 2003.

C. Copy of Reference C103 Provided for Consideration

A copy of reference C103 identified on the Information Disclosure Statement filed September 11, 2003 is provided for consideration.

D. Priority Disclaimed

Applicants have deleted the claim to priority in the specification pursuant to MPEP 201.11, section III. G. at 200-73, entitled "Reference to Prior Applications - Deleting Benefit Claims," which states:

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[1] Note there is a provisional obviousness-type double patenting rejection pending against this claim.

> "As a result of the 20-year patent term [measured from the filing date of the earliest U.S. application for which benefit under 35 U.S.C. 120, 121, or 365(c) is claimed], **it is expected,** in certain circumstances, that applicants may cancel their claim to priority **by amending the specification or submitting a new application data sheet** (no supplemental declaration is necessary) to delete any references to prior applications." *Id.* (emphasis added).

E. Double Patenting Rejection

The Action provisionally rejects claims 30-43 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 70-104 of copending Application No. 09/556,570 in view of March (U.S. Patent 5,552,309).

Because this rejection is provisional, Applicants will submit a terminal disclaimer, if necessary, once either application is otherwise allowable.

F. Claims 30, 34, and 35 Satisfy §112, second paragraph

The Action rejects claims 30, 34, and 35 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as their invention.

Claim 30 has been amended into independent claim format.

Claims 34 and 35 recite a particle concentration of "particles/ml."

G. Claims 30-40 Are Not Anticipated or Rendered Obvious by Condon *et al.*

The Action rejects claims 30-40 under 35 U.S.C. §102(e) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious over Condon *et al.* (U.S. Patent 6,196,944) ("Condon").

For a reference to anticipate a claimed invention, it must teach every element of the claimed invention. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Claim 31 recites, "A purified recombinant adenovirus

composition comprising between 5 x 10^{14} and 1 x 10^{18} adenoviral particles and having between 50 pg and 10 ng of contaminating human DNA per 1 x 10^{12} viral particles."

Condon does not teach a purified adenoviral composition that has "between about 50 pg and 10 ng of contaminating human DNA per 1 x 10^{12} viral particles."

Moreover, contrary to the Action's contentions on page 5, the product disclosed by Condon does not reasonably appear the same as, or similar to, the claimed product. The Action relies on *In re Best*, 562 F.2d 1252, 1255, 195 U.S.P.Q. 430, 433-34 (CCPA 1977). However, it is not appropriate in the present case to place the burden on the patent owner to show that Condon does not teach the same product because the product of Condon was **not** "produced by identical or substantially identical processes" as compared to the claimed product. The specification makes clear that some embodiments of the purification process involved **both** a filtration step and a chromatography step, whereas Condon teaches only a filtration step. See specification Example 6. The specification is replete with data regarding the efficacy of the chromatography step in achieving an adenovirus composition purified to the degree recited in the claims. Consequently, it is inappropriate to invoke *In re Best* and shift the burden of proof to Applicants.

H. Claims 30, 31, 34, 36, and 43 Are Not Obvious over Huyghe

The Action rejects claims 30, 31, 34, 36, and 43 under 35 U.S.C. § 103(a) as being obvious over Huyghe *et al* (WO 96/27677) or Huyghe *et al.*, (*Human Gene Therapy* 6:1403-1416, 1995) (collectively "Huyghe references").

Claim 40 was not rejected over the Huyghe references. A purity limitation consistent with the recitation of claim 40 is indicated in the present claims. Therefore, the present claims should be similarly clear of the Huyghe references.

I. Claims 30-38 and 43 Are Not Obvious over Blanche *et al.*

The Action rejects claims 30-38 and 43 under 35 U.S.C. § 103(a) as being obvious over Blanche *et al.* (WO 98/00524) (U.S. Patent No. 6,485,958) ("Blanche").

Claim 41 was not rejected based Blanche. The claims recite a level of purity that is consistent with the level recited in claim 41. Therefore, all of the pending claims should be free of Blanche.

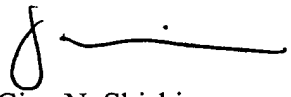
Applicants also note that the specification indicates that the use of Benzonase®—a nuclease used to reduce the amount of contaminating nucleic acid—with 1 M NaCl, as described in Blanche, inhibits enzyme activity. Specification at page 160, lines 20-25.

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is respectfully requested.

Respectfully submitted,



Gina N. Shishima
Reg. No. 45,104
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201
(512) 536-4598 (facsimile)

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